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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,231	08/19/2004	Paul Richard Gellert	ASZD-P01-724	3886

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,231	GELLERT ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 1-18 ARE PRESENTED FOR EXAMINATION

Applicants' amendment filed 5/29/2007 has been received and entered into the application. Accordingly, claims 1, 7, 12, 14, and 17 have been amended and claim 19 has been cancelled.

In view of the above amendments, the rejection of claims 1-19 under 35 U.S.C. 112, 2nd Paragraph has been overcome and thus is *withdrawn*. The following rejections are reiterated and constitute the totality of issues remaining in the present application.

Response to Arguments

Applicant's arguments filed 5/29/2007 have been fully considered but they fail to persuade the Examiner of an error in his determination that the claimed compositions are prima facie obvious in view Gibson (U.S. Patent No. 5,770,599) and Thosar (U.S. Patent No. 6,410,054). Firstly, Applicants' amendments to the claims reciting limitations with respect to the dissolution of the claimed compositions are not pertinent to patentability of the compositions. For example, the recitation of a "wherein" clause reciting specific dissolution characteristics of the claimed compositions do not render any less obvious the *compositions* that are being claimed. This is because the "wherein" clause recited in the instant claims is not a limitation of the claimed composition. The question remains whether or not a composition comprising Iressa and the claimed excipients would have been *prima facie* obvious; the characteristics of such a composition are inconsequential to the subject matter instantly claimed.

Applicants argue that Thosar is limited to formulations of a specific compound (eplerenone), which is essentially pH independent. Accordingly, Applicants assert that it would

not have been *prima facie* obvious to combine a water-soluble cellulose ether (such as hydroxypropyl methylcellulose described in Thosar) with the instantly claimed agent that is pH dependent. This argument is not persuasive because the characteristics of the active agent are not the basis of the *prima facie* case of obviousness presented by the Examiner. The instantly claimed active agent (Iressa) is known in the art and formulated with pharmaceutically acceptable diluents and carriers (Gibson). While Gibson does not explicitly teach specific diluents and carriers, Thosar teaches compositions comprising the instantly claimed excipients. Thosar further teaches that the compositions described therein provide readily soluble forms and "unique combinations" of carrier materials that provide better solubilization characteristics, improved bioavailability, chemical stability, dissolution profiles, disintegration times, and improved pharmacokinetics (col. 2, lines 51-58; col. 3, line 46 to col. 4, line 14). Clearly, it is the carrier materials, not the active agent, that impart such beneficial properties. Further, it is well within the purview of the skilled artisan to substitute one active agent for another in known pharmaceutical formulations. The fact that Thosar teaches hydroxypropyl methylcellulose as a preferred binding agent used to impart cohesive properties to the formulations therein or as a coating material for use in controlled release compositions does not render any less obvious the claimed compositions.

The rejection of claims 1-18 as being obvious over Gibson in view of Thosar is maintained for the reasons of record and reiterated below.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gibson (U.S. Patent No. 5,770,599; Issued Jun. 23, 1998) in view of Thosar *et al.* (U.S. Patent No. 6,410,054; Issued Jun. 25, 2002; Filed Dec. 8, 1999).[1]

The instant claims recite pharmaceutical compositions comprising 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline (*i.e.* Iressa® or gefitinib) and a water-soluble cellulose ether or ester of a water-soluble cellulose ether.

Gibson discloses the instantly claimed compound (col. 8, lines 61-64). It is further disclosed that the compounds exemplified in Gibson can be formulated into pharmaceutical compositions in association with a pharmaceutically acceptable diluent or carrier (col. 13, line 65 to col. 14, line 3; Claim 17). The composition may be in a form suitable for oral administration,

[1] As discussed in the Office Action mailed 8/1/2006, the instant claims are afforded a priority date of June 11, 2002 (filing date of foreign priority document 0213267.8). As such, Gibson qualifies as prior art under 35 U.S.C. § 102(b) and Thosar *et al.* qualify as prior art under 35 U.S.C. § 102(e)(2).

for example as a tablet or capsule (col. 13, lines 4-5). The compositions may be prepared in conventional manners using conventional excipients (*id.* at lines 10-11). The instant claims differ from the Gibson disclosure in that they recite specific excipients and proportions of excipients to active agent.

Thosar *et al.* disclose immediate release formulations of eplerenone so as to provide a readily soluble form of eplerenone (Abstract; col. 2, lines 39-40). The compositions disclosed therein provide "unique combinations" of carrier materials that provide better solubilization characteristics, improved bioavailability, chemical stability, dissolution profiles, disintegration times and improved pharmacokinetics (*id.* at lines 51-58; col. 3, line 46 to col. 4, line 14). The compositions can be formulated in a form suitable for oral administration comprising 1% to 95% active agent (col. 6, lines 40-41 and 44-49). Such oral forms can further comprise buffering agents and can be prepared with enteric coatings (*id.* at lines 62-65). Carriers include agents that improve dissolution and disintegration profiles, hardness, crushing strength and friability (col. 8, lines 29-36). Diluents are present in amounts ranging from 5% to 99% and can include lactose, mannitol and microcrystalline cellulose (*id.* at lines 38-59). Disintegrants are present in amounts ranging from 0.5% to 30% and include celluloses, such as methylcellulose, sodium carboxymethylcellulose and carboxymethylcellulose (col. 9, lines 9-27). Binding agents include povidone, present in an amount of 0.5% to 25% (*id.* at lines 33-55). Hydroxypropyl methylcellulose is a preferred binding agent, present in a range of 0.5% to 10% (*id.* at lines 56-62). Additional excipients are disclosed at col. 10, line 6 to col. 11, line 41. The immediate release compositions preferably release 90% of the active agent within 45 minutes using 0.1 N HCl in water at 37 °C (col. 13, line 65 to col. 14, line 16). Suitable coating materials include

hydroxypropyl methylcellulose as instantly claimed (col. 20, lines 19-27). An immediate release composition comprising active agent and hydroxypropyl methylcellulose is shown in Example 3 (col. 36, lines 25-50). The reference thus teaches immediate release pharmaceutical compositions comprising the instantly claimed excipients.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

In the instant case, Gibson teaches that the instantly claimed compound can be formulated into pharmaceutical compositions comprising conventional excipients. Thosar *et al.* teach that the instantly claimed excipients were known in the art to be useful in immediate release compositions and further suggests that the compositions described therein provide readily soluble forms and "unique combinations" of carrier materials that provide better solubilization characteristics, improved bioavailability, chemical stability, dissolution profiles, disintegration times, and improved pharmacokinetics. As such, one skilled in the art motivated to formulate an immediate release composition of 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline would reasonably expect that the excipients present in the compositions taught in Thosar *et al.* could be predictably used with any active agent, including those taught in Gibson.

As such, absent a demonstration of unexpected results commensurate in scope with the claims, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to formulate a composition of 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline and water-soluble cellulose ethers. The skilled artisan would have been highly motivated to formulate a composition wherein the composition improves bioavailability, stability, dissolution profiles, disintegration times, etc. as taught in Thosar *et al.* With regard to claims that recite specific concentration and ratios of the components, it is the position of the examiner that such limitations do not impart patentability absent a showing of criticality. The prior art discloses compositions comprising the active agent and excipients of the recited claims. Applicant is reminded that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See *In re Aller*, 220 F.2d 454 105 USPQ 233,235 (CCPA 1955).

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

August 14, 2007

Ardin H. Marschel 8/16/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER